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Defining the characteristics and expectations of fluid bolus therapy: A worldwide perspective☆,☆☆,★,★★,☆☆☆

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ABSTRACT

Purpose: The purpose of the study is to understand what clinicians believe defines fluid bolus therapy (FBT) and the expected response to such intervention.
Methods: We asked intensive care specialists in 30 countries to participate in an electronic questionnaire of their practice, definition, and expectations of FBT.
Results: We obtained 3138 responses. Despite much variation, more than 80% of respondents felt that more than 250 mL of either colloid or crystalloid fluid given over less than 30 minutes defined FBT, with crystalloids most acceptable. The most acceptable crystalloid and colloid for use as FBT were 0.9% saline and 4% albumin solution, respectively. Most respondents believed that one or more of the following physiological changes indicates a response to FBT: a mean arterial pressure increase greater than 10 mm Hg, a heart rate decrease greater than 10 beats per minute, an increase in urinary output by more than 10 mL/h, an increase in central venous oxygen saturation greater than 4%, or a lactate decrease greater than 1 mmol/L.
Conclusions: Despite wide variability between individuals and countries, clear majority views emerged to describe practice, define FBT, and identify a response to it. Further investigation is now required to describe actual FBT practice and to identify the magnitude and duration of the physiological response to FBT and its relationship to patient-centered outcomes.

1. Introduction

Fluid bolus therapy (FBT) is one of the most common interventions in intensive care. However, uncertainty exists regarding the strength of the evidence associating FBT with an independent improvement in patient centered outcomes and doubt about the magnitude and duration of its physiological effects [1–4].

Recently, 3 large, multicenter, randomized controlled trials of the management of severe sepsis demonstrated significant differences in the volume of fluid administered over the first 6 hours of the management of sepsis in critically ill patients [5–7]. In addition, other studies have demonstrated little consistency in regional definitions of FBT [8,9]. Furthermore, definitions and clinicians' expectations of the physiological effects of FBT have been shown to vary significantly within a single country [10], whereas the use of hydroxyethyl starch solutions (HES) has become controversial due to reported evidence of harm [11]. However, at an international level, there is little information on self-reported FBT practice, on what defines an FBT, and on the expected physiological effects that would confirm a response to FBT for clinicians. Moreover, substantial difference between stated and recorded practice would indicate a significant degree of cognitive dissonance among intensivists providing this essential medical therapy.

Accordingly, we conducted an international survey of intensive care specialists. Our objectives were to determine their current self-reported practice, their views of what defined FBT, and their assessment of what would constitute a response to FBT.

2. Methods

2.1. Ethics approval

This study was approved by both our local hospital (HREC no. LNR/14/Austin/197) and the Monash University Research Ethics Committee (project no. CF14/2539-2014001354). Completion of the survey questionnaire was deemed to imply consent.

2.2. Survey design and pilot phase

We used an established electronic survey delivered via a commercial Web-based survey instrument (www.SurveyMonkey.net, Palo Alto, CA). We designed a simple questionnaire that could be answered in less than 10 minutes while still providing comprehensive information about the volume, the rate of administration, and the types of fluids used for FBT as well as the expected physiological changes that would define a response to such therapy. This survey was originally piloted in an Australian metropolitan, tertiary referral university hospital and revised before being distributed to Australian and New Zealand intensivists and emergency physicians in a wider pilot project which has since been published [10]. No changes were made as a result of this second pilot phase. The survey is included in the electronic supplemental material (ESM). The survey was in English only.

2.3. Questionnaire

The questionnaire comprised 2 sections, excluding nonidentifying demographic data. The first section of the survey asked respondents to identify (*a*) appropriate fluids for FBT, excluding whole blood or packed red cells; (*b*) the minimum volume of that fluid that constituted a fluid bolus; and (*c*) the maximum amount of time for they would allow for that volume of that fluid to be delivered over while still constituting FBT. The second section contained 6 items; each item asked respondents to identify the minimum change in a specific physiological variable that they believe constituted a response to FBT, when fluid had been given as a response to a deficit in that variable. These questions were designed to make it clear to the respondent that they were to be answered as if the decision to give the bolus had already been made. We deliberately did not assign temporal scales to these expected responses to FBT to isolate the magnitude of changes that clinicians expect from FBT.

2.4. Survey dissemination

An academic intensivist in each participating country was approached directly by the authors to act as a national coordinator. These coordinators invited intensive care specialists in their country to participate in the survey in a variety of ways, including personal and institutional contacts, national societies, and through direct approach at national meetings. Participation was voluntary and anonymous. When directly approached, specialists completed the questionnaire using a tablet computer. Where e-mail was used, an invitation was sent by e-mail containing a hyperlink to the questionnaire. Reminder e-mails were sent subsequently to encourage participation.

2.5. Population data and missing data

Information regarding the population size of each country in 2013 was obtained from publically available data published by the World Bank (http://data.worldbank.org/indicator/SP.POP.TOTL). We included all responses indicating country of origin; those not providing this information were excluded from analysis. Responses were analyzed using the number of respondents completing each individual section of the questionnaire as a denominator. We did not impute missing data; a summary of missing data is presented in the ESM (Table E1).

2.6. Statistical methods

Responses were downloaded from the Web-based survey provider into an MS Excel (Microsoft, Seattle, WA) spreadsheet for storage and graphics creation. Statistical analyses were performed using STATA version 13 (Stata Corp, College Station, TX). Results are presented as the overall proportion of all respondents, with the highest and lowest national rates provided to indicate the range of national responses obtained. The number of respondents who believed a specific fluid was acceptable for use as FBT is used as the denominator when calculating the responses regarding the minimum volume and maximum duration of administration believed to constitute FBT.

3. Results

3.1. National rates of response

Overall, 3138 responses were returned from 30 countries on 6 continents with a combined population of more than 3.9 billion people between August 1 and December 31, 2014. The overall survey response rate was 0.8 responses per million/population, with the lowest national response rate being 0.2 per million (China and India), and the highest 17 (Denmark) (Table 1; Fig. E1 in the ESM). Specialist qualifications in intensive care medicine were held by 73% (2276/3138) of respondents (Table E2), and 52% (1538/2991) of respondents had been practicing as a specialist for less than 10 years (Table E3).

Table 1
Responses by country

Region	Respondents, n (%)	Population, 2013, millions	Response rate, per million/ population
Argentina	123 (4%)	41.5	3
Australia	149 (5%)	23.1	6
Austria	107 (3%)	8.5	13
Belgium	108 (3%)	11.2	10
Brazil	178 (6%)	200.4	1
Canada	106 (3%)	35.2	3
Chile	44 (1%)	17.6	2.5
China	302 (10%)	1357	0.2
Colombia	41 (1%)	48.3	1
Denmark	95 (3%)	5.6	17
England, Wales, and Northern Ireland	67 (2%)	58.4	1
Finland	51 (2%)	5.4	9
France	37 (1%)	65.9	0.5
Germany	178 (6%)	80.7	2
India	182 (6%)	1252	0.2
Italy	203 (6%)	60.2	3
Japan	120 (4%)	127.3	1
Malaysia	27 (1%)	29.7	1
New Zealand	26 (1%)	4.4	6
Saudi Arabia	25 (1%)	28.8	1
Scotland	81 (2.5%)	5.3	15
Singapore	58 (2%)	5.4	11
South Africa	112 (3.5%)	53.2	2
Spain	193 (6%)	46.6	4
Sweden	91 (3%)	9.6	9.5
Switzerland	104 (3%)	8.1	13
The Czech Republic	58 (2%)	10.5	5.5
The Netherlands	25 (1%)	16.8	1.5
The Republic of Ireland	41 (1%)	4.6	9
USA	206 (7%)	316.1	0.5
Total	3138 (100%)	3937.4	0.8

Where number (n) and proportion (%) of respondents are displayed with the 2013 national population data from the World Bank (http://data.worldbank.org/indicator/SP.POP.TOTL).

3.2. Defining FBT

In total, 83% (2616/3138) of respondents completed the first section of the questionnaire, with national completion rates varying from 51% (France) to 96% (New Zealand) (Table E1, ESM).

3.3. Crystalloids as FBT

Overall, 73% of respondents felt 0.9% saline was suitable for use as FBT. German and Austrian physicians found it least acceptable as FBT fluid (26%); and Saudi Arabian physicians, the most (100%). Similar proportions of respondents felt lactated and acetated solutions to be suitable, with similar variability (Table 2).

For all crystalloid solutions, more than 90% of respondents felt that more than 250 mL of fluid had to be given to constitute FBT (Table 3). More than 80% of respondents felt that crystalloid solutions had to be administered in less than 30 minutes to constitute FBT (Table 4).

3.4. Colloid as FBT

Fewer respondents felt that colloid solutions were suitable for use as FBT. Four percent albumin was the most widely accepted colloid (46%), with a range of national responses from 19% (Austria) to 95% (Australia). With only 27% of respondents believing HES to be suitable for use as FBT, it was the least acceptable colloid and fluid overall (Table 2).

Approximately 80% of respondents felt that more than 250 mL of most colloid solutions had to be given to constitute FBT (86% in the case of 6% HES, 79% for 4% albumin, and 87% for gelatins). Only 19% of respondents felt that more than 100 mL of 20% albumin had to be given to constitute FBT (Table 3).

Table 2
Defining the fluids acceptable for use as fluid bolus therapy

Region	4% albumin	20% albumin	HES	Gelatin	0.9% saline	CSL	Acetate	Total
Argentina	32 (31%)	24 (23%)	30 (29%)	33 (32%)	97 (94%)	51 (50%)	53 (51%)	103
Australia	132 (95%)	46 (33%)	6 (4%)	36 (26%)	124 (89%)	112 (81%)	130 (94%)	139
Austria	17 (19%)	29 (32%)	45 (49%)	41 (45%)	24 (26%)	56 (62%)	53 (58%)	91
Belgium	42 (44%)	38 (40%)	41 (43%)	40 (42%)	62 (65%)	80 (84%)	71 (75%)	95
Brazil	62 (41%)	40 (26%)	31 (21%)	17 (11%)	136 (90%)	89 (59%)	101 (67%)	151
Canada	77 (77%)	45 (45%)	13 (13%)	4 (4%)	84 (84%)	83 (83%)	68 (68%)	100
Chile	9 (22%)	20 (49%)	6 (15%)	8 (20%)	36 (88%)	21 (51%)	21 (51%)	41
China	84 (37%)	96 (42%)	104 (45%)	81 (35%)	186 (81%)	137 (60%)	129 (56%)	230
Colombia	12 (39%)	9 (29%)	8 (26%)	4 (13%)	23 (74%)	19 (61%)	24 (77%)	31
Denmark	51 (61%)	45 (54%)	4 (5%)	1 (1%)	76 (90%)	74 (88%)	47 (56%)	84
England, Wales, and Northern Ireland	31 (58%)	23 (43%)	3 (6%)	18 (34%)	31 (58%)	37 (70%)	52 (98%)	53
Finland	23 (49%)	23 (49%)	1 (2%)	2 (4%)	27 (57%)	47 (100%)	23 (49%)	47
France	7 (37%)	6 (32%)	9 (47%)	11 (58%)	18 (95%)	11 (58%)	14 (74%)	19
Germany	38 (25%)	59 (39%)	49 (32%)	57 (38%)	40 (26%)	124 (82%)	80 (53%)	152
India	35 (21%)	21 (13%)	34 (21%)	35 (21%)	130 (80%)	87 (53%)	86 (53%)	163
Italy	54 (36%)	68 (45%)	84 (55%)	83 (55%)	111 (73%)	112 (74%)	92 (61%)	152
Japan	40 (51%)	12 (15%)	19 (24%)	0 (0%)	38 (48%)	63 (80%)	50 (63%)	79
Malaysia	15 (60%)	4 (16%)	4 (16%)	22 (88%)	19 (76%)	16 (64%)	22 (88%)	25
New Zealand	20 (80%)	7 (28%)	0 (0%)	0 (0%)	23 (92%)	24 (96%)	21 (84%)	25
Saudi Arabia	16 (73%)	10 (45%)	3 (14%)	1 (5%)	22 (100%)	13 (59%)	10 (45%)	22
Scotland	37 (51%)	9 (13%)	4 (6%)	38 (53%)	48 (67%)	56 (78%)	66 (92%)	72
Singapore	47 (87%)	13 (24%)	16 (30%)	22 (41%)	47 (87%)	39 (72%)	49 (91%)	54
South Africa	26 (29%)	19 (21%)	55 (62%)	41 (46%)	45 (51%)	68 (76%)	64 (72%)	89
Spain	31 (20%)	61 (40%)	54 (36%)	91 (60%)	143 (94%)	101 (66%)	95 (63%)	152
Sweden	63 (78%)	50 (62%)	8 (10%)	11 (14%)	39 (48%)	77 (95%)	36 (44%)	81
Switzerland	27 (30%)	30 (33%)	26 (29%)	28 (31%)	58 (64%)	70 (77%)	69 (76%)	91
The Czech Republic	17 (33%)	17 (33%)	25 (49%)	27 (53%)	25 (49%)	51 (100%)	42 (82%)	51
The Netherlands	6 (29%)	10 (48%)	3 (14%)	0 (0%)	16 (76%)	13 (62%)	13 (62%)	21
The Republic of Ireland	17 (53%)	12 (38%)	4 (13%)	13 (41%)	22 (69%)	11 (34%)	30 (94%)	32
USA	124 (73%)	77 (45%)	10 (6%)	4 (2%)	158 (92%)	131 (77%)	118 (69%)	171
Overall proportion	1192 (46%)	923 (35%)	699 (27%)	769 (29%)	1908 (73%)	1873 (72%)	1729 (66%)	2616
Highest national proportion	95%	62%	62%	88%	100%	100%	98%	103
Lowest national proportion	19%	13%	0%	0%	26%	34%	44%	139
Median (IQR)	43% (30%-61%)	36% (27%-45%)	21% (11%-35%)	32% (7%-44%)	76% (60%-90%)	73% (60%-82%)	68% (56%-81%)	36% (27%-45%)

Overall proportion calculated as the total number finding that fluid acceptable/the number of respondents answering this section (2616). 4% albumin indicates 4% human albumin solution; 20% albumin, 20% albumin solution; gelatin, 4% succinylated gelatin solution; 0.9% saline, 0.9% sodium chloride solution; CSL, compound sodium lactate solution; acetate, acetated solution, proprietary name Plasmalyte; IQR, interquartile range.

Overall, 80% or more of respondents felt that HES, 4% albumin, or gelatins had to be administered in less than 30 minutes to constitute FBT, but 90% of respondents felt that 20% albumin administered in less than 1 hour constituted FBT (Table 4).

3.5. Defining the expected response to FBT

In total, 76.5% (2400/3138) of respondents completed the second section of the questionnaire, with national response rates varying from 43% to 92.5% (Table 5).

Table 3
Defining fluid bolus therapy by volume

	Volume of fluid					
Fluid type	≥100 mL	>125 mL	>250 mL	>500 mL	>750 mL	>1000 mL
Colloids						
4% albumin						
n (%)	151 (13%)	89 (8%)	732 (63%)	186 (16%)	2 (0%)	10 (1%)
Range	0%-64%	0%-26%	18%-86%	0%-38%	0%-3%	0%-3%
20% albumin						
n (%)	729 (81%)	67 (7%)	98 (10.85%)	8 (1%)	0 (0%)	2 (0%)
Range	48%-100%	0%-21%	0%-33%	0%-9%	0%-0%	0%-3%
HES						
n (%)	55 (8%)	39 (6%)	345 (50%)	221 (32%)	10 (2%)	19 (3%)
Range	0%-50%	0%-25%	0%-100%	0%-55%	0%-9%	0%-33%
Gelatin						
n (%)	49 (7%)	47 (6%)	426 (56%)	198 (26%)	11 (1%)	23 (3%)
Range	0%-24%	0%-50%	0%-100%	0%-100%	0%-5%	0%-100%
Crystalloids						
0.9% saline						
n (%)	56 (3%)	41 (2%)	675 (36%)	731 (39%)	32 (2%)	333 (18%)
Range	0%-21%	0%-10%	8%-84%	7%-71%	0%-5%	0%-40%
Acetate						
n (%)	46 (3%)	39 (2.12%)	654 (35%)	728 (40%)	42 (2%)	334 (18%)
Range	0%-19%	0%-11%	0%-78%	11%-80%	0%-6%	0%-67%
CSL						
n (%)	45 (3%)	35 (2%)	641 (38%)	672 (39%)	34 (2%)	276 (16%)
Range	0%-18%	0%-8%	10%-76%	0%-62%	0%-6%	0%-60%

Range is defined by the lowest and highest rates among the individual national responses.

Table 4
Defining fluid bolus therapy by rate of administration

	Rate of administration					
Fluid type	<10 min	<30 min	<1 h	<2 h	<4 h	<6 h
Colloids						
4% albumin						
n (%)	362 (31%)	574 (49%)	182 (16%)	28 (2%)	11 (1%)	4 (0%)
Range	9%-67%	31%-75%	0%-39%	0%-19%	0%-19%	0%-4%
20% albumin						
n (%)	241 (27%)	437 (49%)	149 (17%)	36 (4%)	25 (3%)	12 (1%)
Range	0%-50%	22%-100%	0%-33%	0%-33%	0%-22%	0%-25%
HES						
n (%)	199 (29%)	355 (52%)	105 (15%)	24 (3.5%)	3 (0%)	1 (0%)
Range	0%-100%	0%-100%	0%-37%	0%-21%	0%-33%	0%-2%
Gelatin						
n (%)	251 (33%)	369 (49%)	116 (16%)	11 (1%)	3 (0%)	4 (1%)
Range	0%-100%	0%-75%	0%-100%	0%-12%	0%-3%	0%-5%
Crystalloids						
Saline						
n (%)	644 (35%)	875 (48%)	251 (14%)	54 (3%)	12 (1%)	7 (0%)
Range	14%-76%	19%-86%	0%-29%	0%-7%	0%-4%	0%-2%
Acetate						
n (%)	603 (33%)	876 (48%)	264 (14%)	64 (4%)	11 (1%)	9 (1%)
Range	12%-76%	22%-82%	0%-33%	0%-11%	0%-5%	0%-3%
CSL						
n (%)	568 (34%)	812 (48%)	223 (13%)	54 (3%)	11 (1%)	11 (1%)
Range	9%-76%	22%-79%	0%-30%	0%-10%	0%-4%	0%-2%

Range is defined by the lowest and highest rates among the individual national responses.

Although variation between individual countries was present, more than 50% of respondents believed that mean arterial pressure (MAP) must increase by 10 mm Hg or more to indicate a response to FBT. Similarly, more than 70% of respondents believed that heart rate (HR) must fall by 10 beats per minute (bpm) or more to constitute a response to FBT. More than 80% believed that central venous pressure must increase by 2 mm Hg or more to constitute a response to FBT. More than 80% believed that urine output (UO) had to increase by 10 mL/h or more, and more than 70% believed that central venous oxygen saturation must improve by 4% or more to constitute a response to FBT. More than 50% of respondents felt that lactate should fall by more than 1 mmol/L to constitute a response to FBT (Table 5).

Table 5
Defining what constitutes a physiological response to fluid bolus therapy

	Overall response, n (%)	Range between countries
Respondents completing this section	2400 (76.5%)	43%-92.5%
What is the minimum change in MAP that you believe constitutes a response to FBT?		
0-5 mm Hg	118 (5%)	0%-22%
5-10 mm Hg	1063 (44%)	24%-67%
10-15 mm Hg	859 (36%)	14%-53%
15-20 mm Hg	248 (10%)	0%-19%
20-25 mm Hg	68 (3%)	0%-10%
>25 mm Hg	44 (2%)	0%-6%
What is the minimum change in HR that you believe constitutes a response to FBT?		
0-5 bpm	63 (2.5%)	0%-11%
5-10 bpm	652 (27%)	5%-47%
10-15 bpm	1020 (42.5%)	22%-59%
15-20 bpm	474 (20%)	5%-29%
20-25 bpm	113 (5%)	0%-19%
>25 bpm	78 (3%)	0%-10%
What is the minimum change in central venous pressure that you believe constitutes a response to FBT?		
0-2 mm Hg	408 (17%)	5%-28%
2-4 mm Hg	1258 (53%)	28%-68%
4-6 mm Hg	523 (22%)	11%-41%
6-8 mm Hg	100 (4%)	0%-14%
8-10 mm Hg	77 (3%)	0%-13%
>10 mm Hg	34 (1%)	0%-6%
What is the minimum change in hourly UO that you believe constitutes a response to FBT?		
0-5 mL/h	97 (4%)	0%-14%
5-10 mL/h	370 (15%)	3%-31%
10-15 mL/h	460 (19%)	4%-34%
15-20 mL/h	487 (20%)	4%-46%
20-25 mL/h	423 (18%)	4%-29%
25-30 mL/h	563 (24%)	6%-48%
What is the minimum change in central venous oxygen saturation that you believe constitutes a response to FBT?		
0%-2%	118 (5%)	0%-11%
2%-4%	513 (21%)	4%-39%
4%-6%	998 (42%)	22%-56%
6%-8%	382 (16%)	8%-39%
8%-10%	225 (9%)	3%-18%
>10%	164 (7%)	0%-22%
What is the minimum change in blood lactate concentration that you believe constitutes a response to FBT?		
0-0.5 mmol/L	258 (11%)	0%-19%
0.5-1 mmol/L	915 (38%)	16%-56%
1-1.5 mmol/L	618 (26%)	16%-39%
1.5-2.0 mmol/L	340 (14%)	0%-24%
2.0-2.5 mmol/L	142 (6%)	0%-12%
>2.5 mmol/L	127 (5%)	0%-26%

Clinician beliefs regarding the minimum physiological changes required after FBT to constitute a response. Range between countries is defined by the lowest and highest rates among the individual national responses.

4. Discussion

4.1. Statement of key findings

We surveyed an international cohort of more than 3000 intensivists in 30 countries and identified significant variation in self-reported FBT practice within and between different countries. However, clear majority trends emerged: crystalloids are preferred over colloids; a volume greater than 250 mL given over less than 30 minutes defines an episode of FBT and, finally, each one or more of these: MAP increase greater than 10 mm Hg, an HR decrease greater than 10 bpm, an increase in UO greater than 10 mL/h, and a drop in lactate concentration greater than 1 mmol/L was reported to define a response to FBT.

4.2. Relationship with previous studies

International variability in the documented practice of FBT is established. However, in the FENICE study, the median volume of fluid administered was 500 mL over approximately 30 minutes with crystalloids used in preference [9]. A study of 2694 episodes of FBT in 777 patients across 19 French intensive care units (ICUs) suggested that a median of 3 boluses are given per patient, also with marked variability in the rate and volume of FBT [8]. The most commonly used fluid was 0.9% saline. In contrast to these European studies, an observational study in an Australian ICU found that 750 mL of, most commonly, 4% albumin solution was given most often for FBT, with FBT contributing to more than 50% of fluid balance on the first ICU day [12]. A previous cross-sectional survey of patients receiving fluid resuscitation in 391 ICUs in 25 countries in 2007 found that more than 50% of patients received FBT on the day of their admission, with more than 30% still receiving FBT on day 6 [13].

Even among albumin users such as Australian and New Zealand, colloid consumption has also been falling compared to crystalloid use [14], likely due to the reduction in the use of HES, as a consequence of emerging high-level randomized evidence of harm [11,15–17]. Albumin solutions have been shown to be safe in critically ill patients without traumatic brain injury [18,19] and may be beneficial in patients with septic shock [20,21]. Concentrated 20% solutions of albumin may offer safe and effective small volume FBT given concerns regarding fluid overload and patient outcome [22], although they appear to be infrequently used [8,9]. However, they can be more than 100 times more expensive

than 0.9% saline in some countries, and it is possible that clinical equipoise regarding their safety persists [23,24]. There is no high level evidence for the use of gelatine solutions [25].

Several studies have indicated that hypotension, low UO, and markers of inadequate tissue perfusion such as low mixed venous oxygen saturations or a rising lactate trigger FBT [8,9,12,13]. Thus, the use of these features to indicate a response, as seen in our survey, is logical. However, we found substantial variability both within and between countries regarding the physiological changes required to constitute a response to FBT and that stated expectations appear to be divorced from current evidence. A recent pharmacodynamic assessment of the cardiovascular effects of FBT demonstrated that the modest effects of 250 mL of crystalloid delivered as 5 50-mL boluses over 5 minutes on cardiac output peak after 1 minute and dissipate within 10 minutes, regardless of fluid responsiveness [26]. In our study, although most respondents felt that a 10 mm Hg increase in MAP indicated a response to FBT, in a recent systematic review, the median change reported post-FBT was 7 mm Hg immediately after and 3 mm Hg at 60 minutes [4]. Similarly, although most respondents aimed for a greater than 10 bpm decrease in HR after FBT, a median decrease of 2 bpm immediately post-FBT and 1 bpm at 60 minutes has been reported [4]. The effects of FBT on UO are poorly described in the literature but range from a 40 mL/h decrease to a 13 mL/h increase [4]; most intensivists believed that UO had to increase by more than 10 mL/h to show a response. This separation between the physiological effects of FBT reported in the literature and the expectations of the respondents was present across all hemodynamic parameters [4,26].

4.3. Study implications

The findings of this survey demonstrate that most intensivists define FBT as a bolus of more than 250 mL of either colloid or crystalloid fluid given over less than 30 minutes and a response to FBT as an MAP increase greater than 10 mm Hg, an HR decrease greater than 10 bpm, and an increase in urinary output by more than 10 mL/h. Such operative definitions of FBT and response to FBT now allow studies of the epidemiology of FBT in hospitals and of the response rate to such intervention. This is likely important because 25 to more than 200 million separate exposures to intravenous fluids could occur in the United States alone each year [27,28].

In 7 of 30 countries, more than 40% of respondents and 27% of all respondents believed 6% HES solution to be acceptable for use as FBT (Table 2). This is substantially higher than the 16% reportedly not avoiding HES use in the international survey component of the systematic review [29]. This is despite high-level randomized controlled trials [15–17] and meta-analyses [11,30] demonstrating harm as well as widespread concern and regulatory body warning regarding HES use in critically ill patients.[31].

4.4. Study strengths and limitations

Our study has several strengths. First, this is the largest international FBT survey of individual intensivists to date, with the breadth of international involvement offering significant external validity. Second, FBT is a ubiquitous but surprisingly unexplored aspect of critical care management. Third, our findings provide insight into the national and international variation that exists in FBT practice. Fourth, it is the first to document both the variation in the physiological response that clinicians internationally expect from FBT and the separation that exists between these and the responses described in the literature. Fifth, we subjected our survey to a robust assessment pre-release, using expert review, a piloted trial, and a binational trial published in a peer-reviewed journal [10] to refine our approach.

This study also has some limitations. First, as a voluntary survey of self-reported practice, our results do not necessarily represent actual practice. However, several studies have demonstrated acceptable correlations between self-reported and documented practice with such self-reporting being likely to be useful in representing a spectrum of clinical behavior [32,33]. Second, given our method of survey dissemination, we cannot impute an appropriate denominator to calculate a response rate; however, given the variability of the responses, even if significant selection bias was present, it is likely that practice internationally is even more variable than is reported by the respondents. Third, a varying number of respondents in each country ceased their progression through the survey at various points. This may reflect the fact the survey was only presented in English or the complex and polarizing nature of studies examining fluid administration. Documented delivery of FBT suggests international variation in practice, and it may be that our descriptions of the therapy or expected response were incompatible with local practice patterns [9,13]. The lack of an associated timeframe regarding response to FBT may have resulted in confusion; however, we were seeking an objective, quantitative measure of the maximal response to FBT. To this end, more subjective clinical markers of response to FBT, such as skin mottling or capillary refill time, were omitted. Alternatively, the term *response* may have been felt to be unclear, and some respondents may have felt the terminology could have encompassed both positive and negative changes in the variable being investigated. The presentation of responses as discrete incremental changes may have limited the accuracy of responses. Fourth, we did not undertake formal reliability testing. However, more than 3000 clinicians from 30 countries participated in this study, making it the largest assessment of individual practice in the critical care literature and providing the first available global assessment of the characteristics and expectations of FBT in this setting.

5. Conclusions

In an international survey, we found major interindividual and intercountry variations in self-reported FBT and the expected physiological changes that define a response to FBT. However, clear majority views emerged to define FBT and a response to such therapy. Such definitions now enable a more systematic study of the epidemiology of FBT use, the response rate to FBT, the duration of such a response, and the impact on patient-centered outcomes.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.jcrc.2016.05.017.

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